

**Amendment and Response to Restriction Requirement**

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Applicant(s): Kinch et al.

Serial No.: 09/640,935

Confirmation No.: 3254

Filed: 17 August 2000

For: EPHA2 AS A THERAPEUTIC TARGET FOR METASTATIC CANCER (As Amended)

60. The method of claim 58 wherein said administration inhibits proliferation of the metastatic cells.

61. The method of claim 58 wherein said administration reduces invasiveness of the metastatic cells compared to untreated metastatic cells.

62. A method for treatment of a patient having a metastatic tumor, said tumor comprising a population of metastatic cells that express EphA2, said method comprising administering to the patient a therapeutically effective amount of an EphA2 agonist, wherein said administration impedes proliferation of said metastatic cells.

63. The method of claim 62 wherein the metastatic cells overexpress EphA2 as compared to normal cells.

64. A method for treatment of a patient having a metastatic tumor, said tumor comprising a population of metastatic cells that express EphA2, said method comprising administering to the patient a therapeutically effective amount of an EphA2 agonist that increases the phosphotyrosine content of EphA2 in said metastatic cells as compared to untreated metastatic cells.

65. The method of claim 58 wherein the metastatic cells overexpress EphA2 as compared to normal cells.

66. A method for reducing the invasiveness of a metastatic cancer cell that expresses EphA2, the method comprising contacting the metastatic cell with an EphA2 agonist, thereby reducing the invasiveness of the metastatic cell compared to an untreated metastatic cell.

67. The method of claim 66 wherein the metastatic cell overexpresses EphA2 as compared to a normal cell.

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68. The method of claim 66 wherein the metastatic cell is present in a mammalian patient.

69. A method for reducing the proliferative behavior of a metastatic cancer cell that expresses EphA2, the method comprising contacting the metastatic cancer cell with an EphA2 agonist, thereby reducing the proliferative behavior of said metastatic cell compared to an untreated metastatic cell.

70. The method of claim 69 wherein the metastatic cell overexpresses EphA2 as compared to a normal cell.

71. The method of claim 69 wherein the metastatic cell is present in a mammalian patient.

72. A method for treatment of a patient having a metastatic tumor, said tumor comprising a population of metastatic cells that express EphA2, said method comprising administering to the patient a therapeutically effective amount of an EphA2 agonistic antibody wherein said administration reduces metastasis.

73. The method of claim 72 wherein the metastatic cells overexpress EphA2 as compared to normal cells.

74. The method of claim 72 wherein said administration inhibits proliferation of the metastatic cells.

75. The method of claim 72 wherein said administration reduces invasiveness of the metastatic cells compared to untreated metastatic cells.

76. The method of claim 72 wherein the agonistic antibody is a monoclonal antibody.

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77. The method of claim 76 wherein the monoclonal antibody is humanized.

78. The method of claim 76 wherein the monoclonal antibody is conjugated to a cytotoxic agent.

79. A method for treatment of a patient having a metastatic tumor, said tumor comprising a population of metastatic cells that express EphA2, said method comprising administering to the patient a therapeutically effective amount of an EphA2 agonistic antibody, wherein said administration impedes proliferation of said metastatic cells.

80. The method of claim 79 wherein the metastatic cells overexpress EphA2 as compared to normal cells.

81. The method of claim 79 wherein the agonistic antibody is a monoclonal antibody.

82. The method of claim 81 wherein the monoclonal antibody is humanized.

83. The method of claim 81 wherein the monoclonal antibody is conjugated to a cytotoxic agent.

84. A method for treatment of a patient having a metastatic tumor, said tumor comprising a population of metastatic cells that express EphA2, said method comprising administering to the patient a therapeutically effective amount of an EphA2 agonistic antibody that increases the phosphotyrosine content of EphA2 in said metastatic cells as compared to untreated metastatic cells.

85. The method of claim 84 wherein the metastatic cells overexpress EphA2 as compared to normal cells.

86. The method of claim 84 wherein the agonistic antibody is a monoclonal antibody.

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87. The method of claim 86 wherein the monoclonal antibody is humanized.

88. The method of claim 86 wherein the monoclonal antibody is conjugated to a cytotoxic agent.

89. A method for reducing the invasiveness of a metastatic cancer cell that expresses EphA2, the method comprising contacting the metastatic cell with an EphA2 agonistic antibody, thereby reducing the invasiveness of the metastatic cell compared to an untreated metastatic cell.

90. The method of claim 89 wherein the metastatic cell overexpresses EphA2 as compared to a normal cell.

91. The method of claim 89 wherein the metastatic cell is present in a mammalian patient.

92. The method of claim 89 wherein the agonistic antibody is a monoclonal antibody.

93. The method of claim 92 wherein the monoclonal antibody is humanized.

94. The method of claim 92 wherein the monoclonal antibody is conjugated to a cytotoxic agent.

95. A method for reducing the proliferative behavior of a metastatic cancer cell that expresses EphA2, the method comprising contacting the metastatic cancer cell with an EphA2 agonistic antibody, thereby reducing the proliferative behavior of said metastatic cell compared to an untreated metastatic cell.

96. The method of claim 95 wherein the metastatic cell overexpresses EphA2 as compared to a normal cell.

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97. The method of claim 95 wherein the metastatic cell is present in a mammalian patient.

*Ant*  
*CR* 98. The method of claim 97 wherein the agonistic antibody is a monoclonal antibody.

*B<sub>1</sub>* 99. The method of claim 97 wherein the monoclonal antibody is humanized.

100. The method of claim 97 wherein the monoclonal antibody is conjugated to a cytotoxic agent.

101. The method of any one of claims 58, 62, 64, 66 or 69 wherein the population of cells comprises cells selected from the group consisting of breast cancer cells, prostate cancer cells, lung cancer cells and colon cancer cells.

102. The method of any one of claims 72, 79, 84, 89 or 95 wherein the metastatic cancer cell is a cell selected from the group consisting of a breast cancer cell, prostate cancer cell, lung cancer cell and colon cancer cell.

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